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KANSAS CITY, MO 64110

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14. ABSTRACT
Even though commercial bone cements have not significantly changed in the past 50 years and have been used throughout the world, there are significant drawbacks with the current systems. We have developed a silorane based resin superior to polymethyl methacrylate (PNMA) with many improved properties such as significantly less polymerization stress although an associated reduction in mechanical properties. The specific aims for this project are: Specific Aim 1: Develop a silorane bone cement suitable for in vivo studies and to optimize the formulation of the chemically and mixed cured cement prototypes. Specific Aim 2: Determine the biocompatibility properties and wear debris generation of silorane bone cement prototype. Specific Aim 3: Determine the biological response to silorane bone cement prototype in animal models. By addressing the shortcomings of current PMMA bone cement, the development of the novel silorane bone cement will result in a paradigm shift in orthopedic biomaterials.

15. SUBJECT TERMS- bone cement, silorane, prosthetic

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Table of Contents

Yearly Report

Award No.: W81XWH-11-1-0805

Report Date: October 19, 2013

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Principal Investigator: Dr. David Eick (corresponding PI: Dr. Lynda Bonewald)

Award Organization: University of Missouri-Kansas City

Project Title: Bone Repair and Military Readiness

INTRODUCTION:

Even though commercial bone cements have not significantly changed in the past 50 years and have been used throughout the world, there are significant drawbacks with the current systems. These include toxicity, contraction with polymerization, and heat generation. We have developed a silorane based resin superior to polymethyl methacrylate (PMMA) with many improved properties such as significantly less polymerization stress without an associated reduction in mechanical properties. These new resins do not generate cytotoxicity, antigenicity, polymerization stress or significant heat generation. In addition, it appears that this new bone cement is actually supportive of new bone formation. Orthopedic surgeons have had to adapt surgical techniques to account for issues with cementing total joint prostheses and subsequent total joint failures. The cement-bone interface is problematic, as there is no true bonding of cement to bone, only interlay in the trabecular spaces. A cement that can achieve true integration with the bone surface would be advantageous in that it would improve stress transfer to bone and decrease particulate wear. This integration, in turn, could result in improved bone stock if the need for revision arises. Bone infection with prosthetic devices is an increasing major medical problem. As the proposed bone cement prototype polymerizes at a much lower temperature, antibiotics that are sensitive to heat can be added to the cement. Currently, only tobramycin, gentamycin and vancomycin are heat-stable and survive the heat generated by commercially available bone cement during polymerization. Therefore, a wider spectrum of antibiotic availability in bone cement may allow for more appropriate treatment of patients. By addressing the shortcomings of current PMMA bone cement, the development of the novel silorane bone cement will result in a paradigm shift in orthopedic biomaterials.

Keywords: bone cement, silorane, prosthetic

The specific aims for this project are:

Specific Aim 1: Develop a silorane bone cement suitable for *in vivo* studies and to optimize the formulation of the chemically and mixed cured cement prototypes.

Specific Aim 2: Determine the biocompatibility properties and wear debris generation of silorane bone cement prototype.

Specific Aim 3: Determine the biological response to silorane bone cement prototype in animal models.

Original Task Timeline

FY10 Task 1 Develop a silorane bone cement suitable for in vivo studies and to optimize the formulation of the chemically and mixed cured cement prototypes, Subtask 1a. Silanization of filler particles. Months 1-12.

FY10 Task 1: Develop a silorane bone cement suitable for in vivo studies and to optimize the formulation of the chemically and mixed cured cement prototypes, Subtask 1b. Optimize composite formulation with respect to mechanical/handling properties. Months 13-24.

FY10 Task 2: Determine the biocompatibility properties and wear debris generation of silorane bone cement prototype, Subtask 2a. Determine biocompatibility of the optimized chemically initiated silorane bone cement identified in Specific Aim 1 with relevant cell lines (i.e., MLO-A5, MSCs, L929, and HUVEC). Months 1-24.
FY10 Task 3: Determine the biological response to silorane bone cement in animal models, Subtask 3a. Small Animal (Rat) Model. Months 13-18
FY10 Task 3. Determine the biological response to silorane bone cement in animal models, Subtask 3b. Large Animal (Swine) Model. Months 16-24.

Revised Task Timeline

FY10 Task 1 Develop a silorane bone cement suitable for in vivo studies and to optimize the formulation of the chemically and mixed cured cement prototypes, Subtask 1a. Silanization of filler particles. Months 1-12.
FY10 Task 1: Develop a silorane bone cement suitable for in vivo studies and to optimize the formulation of the chemically and mixed cured cement prototypes, Subtask 1b. Optimize composite formulation with respect to mechanical/handling properties. Months 13-24.
FY10 Task 2: Determine the biocompatibility properties and wear debris generation of silorane bone cement prototype, Subtask 2a. Determine biocompatibility of the optimized chemically initiated silorane bone cement identified in Specific Aim 1 with relevant cell lines (i.e., MLO-A5, MSCs, L929, and HUVEC). Months 1-27.
FY10 Task 3: Determine the biological response to silorane bone cement in animal models, Subtask 3a. Small Animal (Rat) Model. Months 13-24
FY10 Task 3. Determine the biological response to silorane bone cement in animal models, Subtask 3b. Large Animal (Swine) Model. Months 24-30.

Revised Gantt Chart

Task	Y1Q1	Y1Q2	Y1Q3	Y1Q4	Y2Q1	Y2Q2	Y2Q3	Y2Q4	Y3Q1	Y3Q2	Status
Specific Aim 1 a											Completed
b											Completed
Specific Aim 2 a											Extended
Specific Aim 3 a											Completed
b											Extended

Green = Completed
Blue = Extended

OVERALL PROJECT SUMMARY:
Progress for year two from end of year one to date:

FY10 Task 1 Develop a silorane bone cement suitable for in vivo studies and to optimize the formulation of the chemically and mixed cured cement prototypes, <u>Subtask 1a. Silanization of filler particles.</u> Months 1-12. COMPLETED.

This task has now been completed. As the major issue was the reduced pullout strength of the silorane bone cements *in vivo* (see Task 3a, Figure 7), we were no longer focusing on silanization of filler particles, rather on improving polymerization properties of the silorane bone cements in a wet environment. While silanation had been observed to produce greater composite mechanical strengths, issues with curing were providing inconsistency to the properties. One potential issue was initial moisture and its effect on the cement curing.

A study to investigate moisture effects and metal implant surface modification effects were done (Table 1, Figure 1). Moisture content in the initial formulation was measured and varied through saturation with water and by drying to low moisture concentrations to observe the effect on moisture. As synthesized and utilized Silmix in all trials to date had moisture contents near saturation, ~1.8%, whereas a saturated moisture concentration was ~1.9%. Azeotropic drying reduced initial moisture content to 1.0 (dried) and 0.3% (ultra-dried), respectively. Curing of these Silmix materials showed variation of cure rate, final cure extent, and strength, which were optimized in rate, extent, and strength by a moderate moisture content. Near saturated moisture provided lowest rates, extents, and final mechanical strengths. Moisture, if controlled in the initial formulation, is ideal for the cement since moisture diffused into the Silmix slowly and low concentrations in the Silmix accelerate polymerization and strength. These results have been borne out with in vivo rat bone pull out strengths, which show consistent, high strength.

Table 1. Karl Fischer titration results for as received Silmix, water saturated Silmix, dried and ultra-dried Silmix resin formulations.

Entry	Formulation Description	Average water, weight% (mg/g) ± Standard Deviation
1	Ultra-Dried SM	**0.0291 ± 0.0057**
2	Dried SM	**0.1029 ± 0.0082**
3	As-Received SM	**0.1781 ± 0.0165**
4	Saturated SM	**0.1932 ± 0.0133**

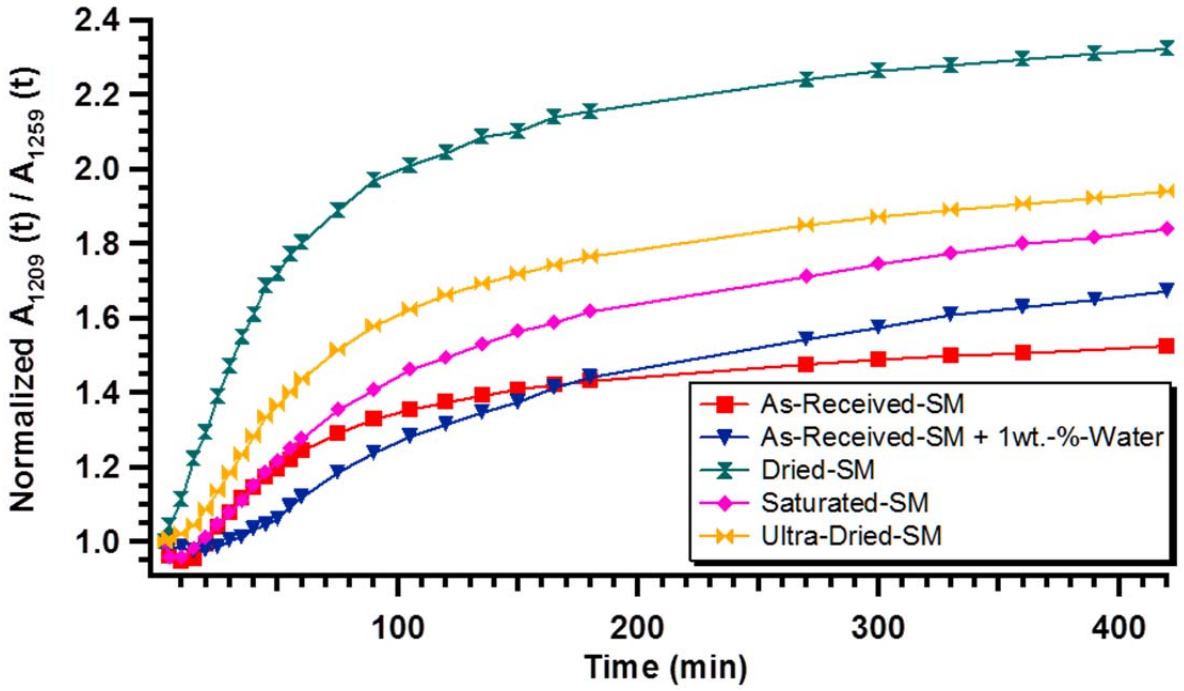


Figure 1. Cure extent, measured as relative FTIR absorption of oxirane to ether band conversion as a function of time, of the Silmix polymerization as a function of water concentration in the initial formulation (per Karl Fischer titration results reported in Table 1).

Conclusion: The DY5-1TOSU system of glass powder-surface silanation composition appears optimal. The system shows consistently higher strengths and metal-bone adhesion strength upon proper control of the initial formulation moisture content. Silanation with 1TOSU provides dry, organic interface particles that are readily dispersed into Silmix and support high strength, high extent composite cure.

FY10 Task 1: Develop a silorane bone cement suitable for in vivo studies and to optimize the formulation of the chemically and mixed cured cement prototypes, Subtask 1b. Optimize composite formulation with respect to mechanical/handling properties. Months 13-24. COMPLETED

Due to some inconsistencies with the co-monomer SilMix system, we instituted a systematic study including quality control of the synthesis and analysis was initiated to determine the reasons. We tested the order of the addition of the reagents for the synthesis of PHEPSI, the impurities of Wilkinson's catalyst (supplier – 97%; trace metals are different), water content, and purification/chromatography of the PHEPSI. We found there was a difference in the polymerization of the samples depended on the amount of water in the monomers and the types of trace metals in the Wilkinson's catalyst. This information was incorporated into the current methods used for the synthesis of the co-monomers.

Investigation of polymerization in wet environment:

After receiving less than optimal pull out results for the live animal study (See Task 3a, Figure 7), an investigation into materials polymerization in damp/wet environments was initiated using the two formulations; an original and a putty. It was found that a wet environment slowed the polymerization by

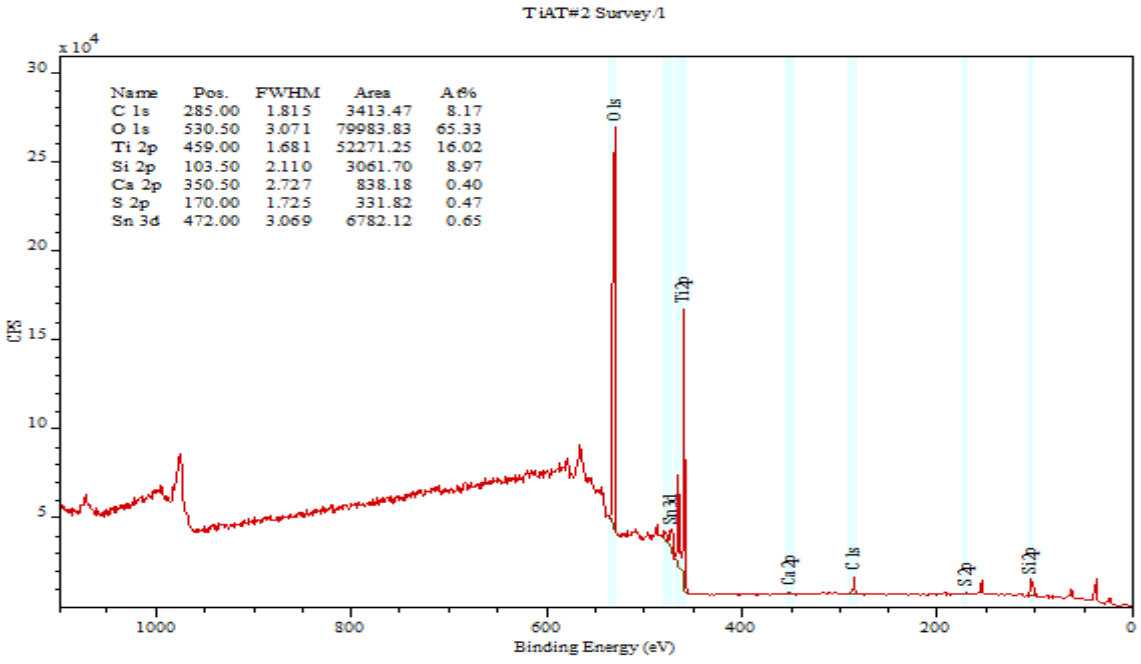
15 min or more depending of the formulation of the material.

Treatment of Ti rods:

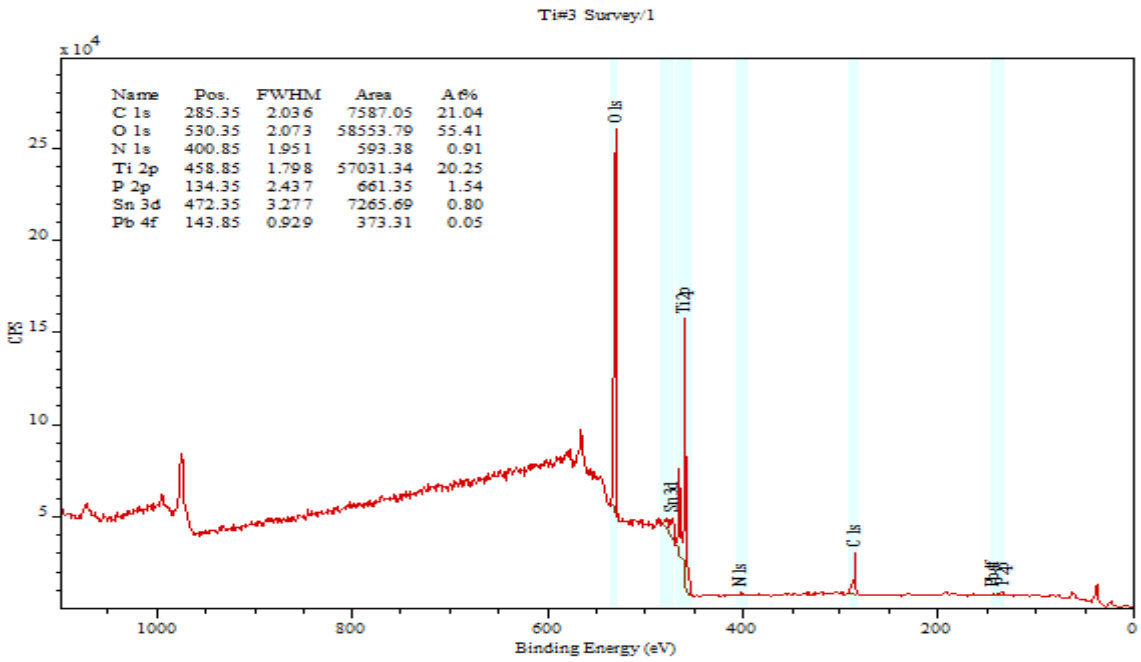
Synthesis of the Ti rod modification: MS&T. The phosphonate ester was first synthesized using an Arbuzov synthesis of epibromohydrin with trimethylphosphite or triethylphosphite. The triethylphosphite was a cleaner and higher yielding reaction due to the higher boiling point of the product (~102 °C at 1.5 mm Hg) and byproduct ethylbromide. Therefore, the reaction progress was followed by TLC with subsequent reduced pressure and distillation of the product.

Deposition process at UMKC: After standard acid treatment, the implants were boiled in UPW for an hour, and removed hot to dry. Samples were sonicated in a solution (46 mL) containing 94% toluene, 4% trimethylsilylbromide, and 2% phosphonate ester (by wt%) at 78-80 °C for 30 min. After 30 min, the sonication was discontinued. Ethanol (4 mL) was added dropwise over 20 min while gently stirring at 78-80 °C. The solution was then for heated an additional 10 min in the water bath. The rods were removed from the solution and washed thoroughly with ethanol. The rods were then placed in 70% ethanol for sterilization. The rods were then tested *in vivo* (see Figure 9). After the *in vivo* testing, SEM and EDS were performed on the treated and untreated rods. There was no phosphorus on the either of the types of rods. This meant the deposition procedure was ineffective.

Surface modifications as performed at MS&T: A surface modification of the titanium (or any transition metal surface) was investigated as part of the silanation/interface control subtask. Surface modification utilizing an epoxy phosphonate ester was readily achieved, characterized (Figure 2), and tested with titanium rod implantation bone pull out strength. It was decided that surgeons would not utilize a surface modified implant, and the work discontinued.



a)



b)

Figure 2. XPS survey spectra of acid-etched titanium metal (a) and DEOMP modified titanium metal (b) showing surface atomic concentrations that demonstrate monolayer phosphonate surface modification of titanium metal surface. Monolayer of phosphate is approximately equivalent to ~1% surface atomic concentration.

Investigate the optimal dual cure initiation system for neat SilMix and paste/putty formulations: Formulations with filler amounts ranging from 65% to 75% and LMC ranging from 0.32% to 0.70% were investigated. The samples were tested in two ways, polymerization time and handling properties. The two best formulations were then tested *in vivo* (see Figure 10). The optimal formulations were a thick material with 74% filler and 0.35% LMC along with a thinner putty with 65% filler and 0.40% LMC.

Investigate the pre-coating of the Ti rods with SilMix: Rods that had been pre-dipped in SilMix were investigated for potential use in the *in vivo* studies. Rods were dipped in either regular SilMix, SilMix with the light initiation system (LCSM), or Putty A (65% DY5-1TOSU/0.40% LMC). It was found that it is best to use the filled material with LMC because it will begin to set up and stick to the rod. Also the material on the rod should not be allowed to completely polymerize before it is inserted. Pre-dipping the rod in Putty A was tested *in vivo* (see Figure 11). No significant differences were seen with or with-out dipping the titanium rod for pre-coating before insertion.

Conclusion: The optimal system is composed of the 65 wt% DY5-1TOSU, 0.40 wt% LMC, and 34.60 wt% LCSM using dry filler and dry co-monomers (in vivo results Task 3a Figure 11).

FY10 Task 2: Determine the biocompatibility properties and wear debris generation of silorane bone cement prototype, Subtask 2a. Determine biocompatibility of the optimized chemically initiated silorane bone cement identified in Specific Aim 1 with relevant cell lines (i.e., MLO-A5, MSCs, L929, and HUVEC). Months 1-27. COMPLETED EXCEPT FOR WEAR DEBRIS EXPERIMENTS.

Within the next 3 months wear debris experiments will be performed with the silorane bone cement DY5-1TOSU for comparison to commercially available bone cement.

FY10 Task 3: Determine the biological response to silorane bone cement in animal models, <u>Subtask 3a. Small Animal (Rat) Model.</u> Months 13-24 COMPLETED EXCEPT FOR HISTOLOGICAL ANALYSES.

1). Rat in vivo study for examination of inflammatory response one week post surgery, and determination of osseointergration and pull-out strength 8 weeks post surgery using commercial bone cement Simplex P, and silorane-based M12-ECHE, DY5-ECHE, DY5-1TOSU bone cements.
For the first in vivo study, sixty six 6-month-old rats were used, twenty two for Simplex P, fourteen for M12-ECHE, fifteen for DY5-ECHE and fifteen for DY5-1TOSU cement. The rats were anesthetized and operated on under aseptic condition. Briefly, the right knee was exposed and a hole was drilled between the femoral condyles and into intramedullary canal. The bone marrow was disrupted. The marrow cavity was irrigated and filled with commercial bone cement Simplex P, silorane-based M12-ECHE, DY5-ECHE, DY5-1TOSU bone cement, respectively. These cements had previously been shown to have the optimal pull-out strength ex vivo. Then a titanium rod, 22 mm long and 1.5 mm in diameter was inserted. The capsule and skin were sutured. The wounds of the knees of rats were not inflamed post surgery. For short term study to examine the inflammatory response, the rats were sacrificed at week one post operation (PO). For long term study to determine the osseointegration and biomechanical strength, the rats were sacrificed at week eight PO. Prior to sacrifice, the body weight of rats was weighed at week 1, 2, 4, 6 and 8 PO and compared to that before surgery. The X-rays of femora of rats were taken at week 1, 4 and 8 PO. Injection of fluorochromes intraperitoneally with tetracycline hydrochloride, alizarin red A, and calcein were performed at 2, 4, and 6 weeks PO.
Change in body weight: The body weight of rats in Simplex P group was dramatically and significantly decreased at week one PO. (Figure 3). No significant reduction in weight was observed for the silorane bone cements. Statistically significant differences between simplex P and silorane-based bone cements groups ($P<0.001$).

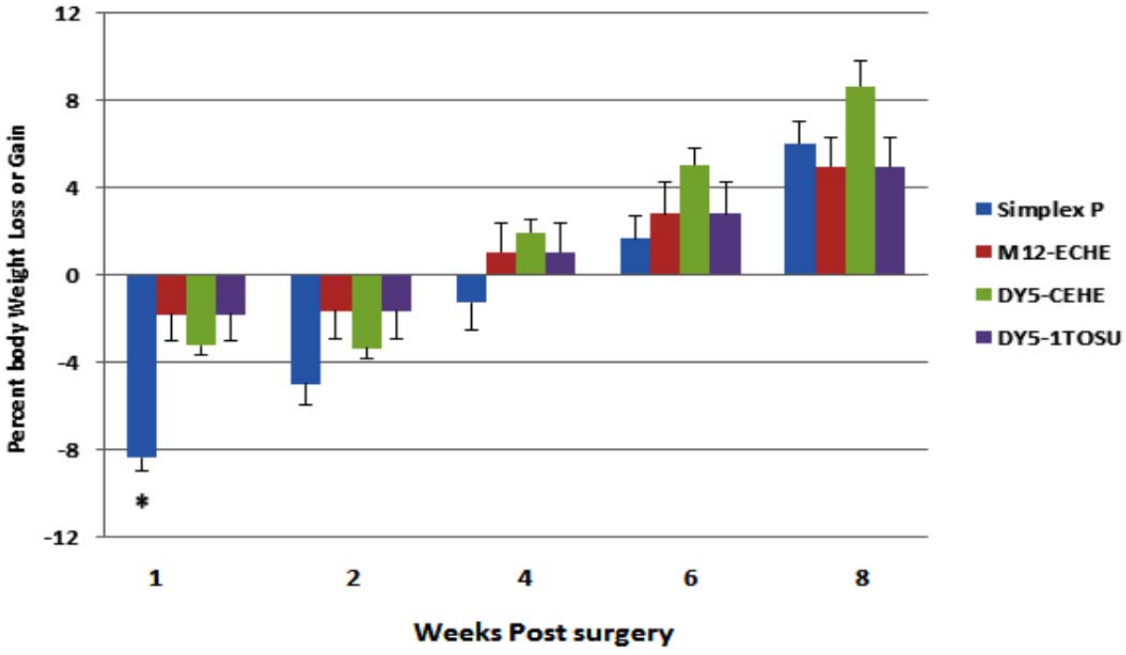


Figure 3. The changes of body weight of rats with commercial bone cement Simplex P, and silorane-based M12-ECHE, DY5-ECHE, DY5-1TOSU bone cement at different time points PO. *$P<0.001$.

Radiographic examination: The radiography of femora of rats treated with different bone cements were performed at week 1, 4 and 8 PO. The radiographs of rat femora filled with commercial bone cement Simplex P showed periosteal reaction at week 4 and 8 PO in contrast to silorane-based M12-ECHE, DY5-ECHE and DY5-1TOSU bone cements (Figure 4).

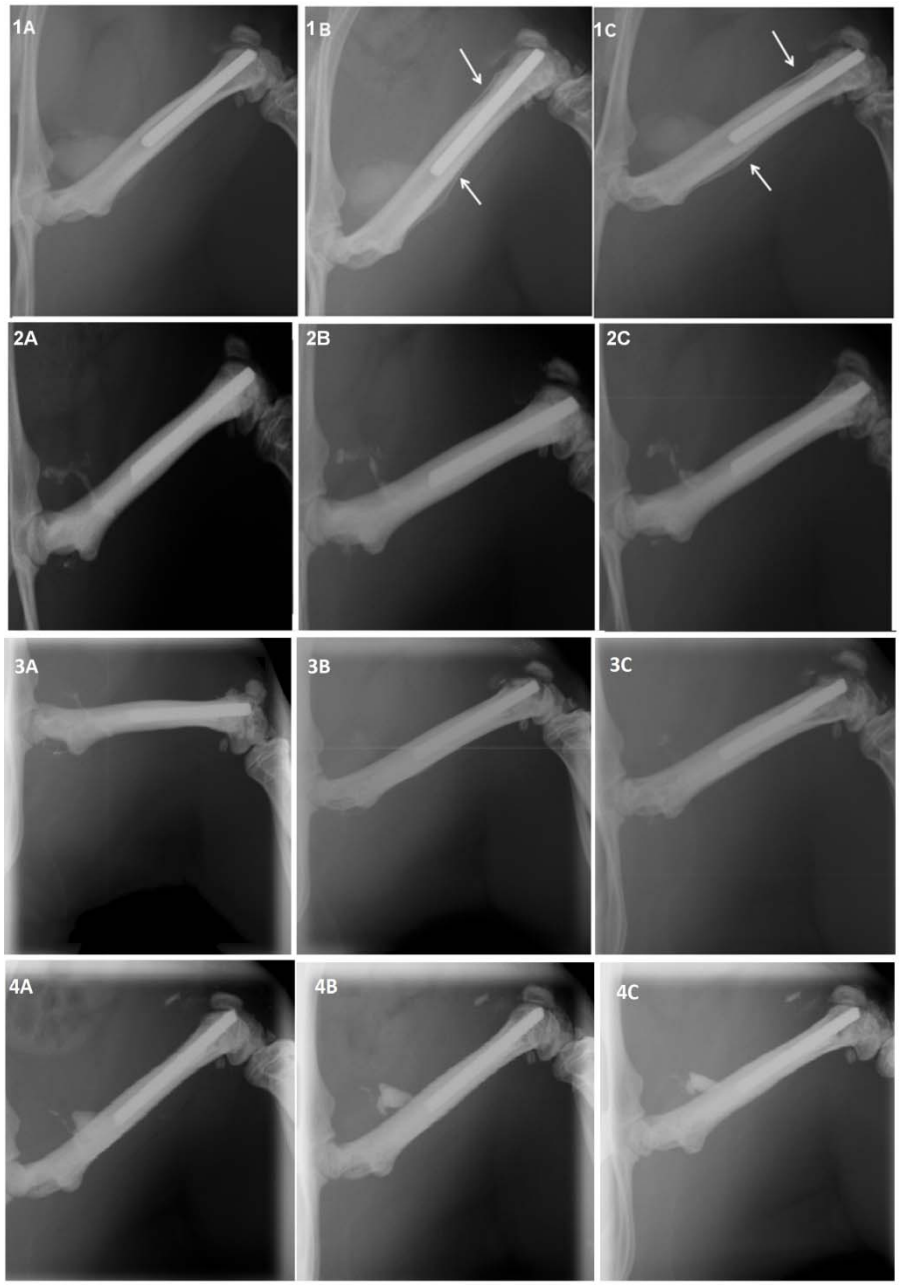


Figure 4. Radiographs of rat femora filled with different bone cements taken at 1 (A), 4 (B) and 8 (C) weeks PO. The images 1A, 1B and 1C represent the rat femur filled with commercial bone cement Simplex P and images of 2A, 2B and 2C with M12-ECHE, images of 3A, 3B and 3C with DY5-1TOSU and images of 4A, 4B and 4C with DY5-ECHE silorane bone cement. A periosteal reaction (arrows) of

rat femur filled with commercial bone cement Simplex P was observed at week 4 (1B) and 8 (1C) PO. There was no periosteal reaction in silorane-based cement groups.

Histological examination: The rats were sacrificed at 1 and 8 weeks PO and the femora were harvested and processed for histology. The femora of rats filled with Simplex P or DY5-1TOSU cement and sacrificed at week one PO were processed, sectioned and stained with H&E. The histological examination shows that there are many inflammatory cells next to commercial bone cement Simplex P in contrast to DY5-1TOSU cement (Figure 5).

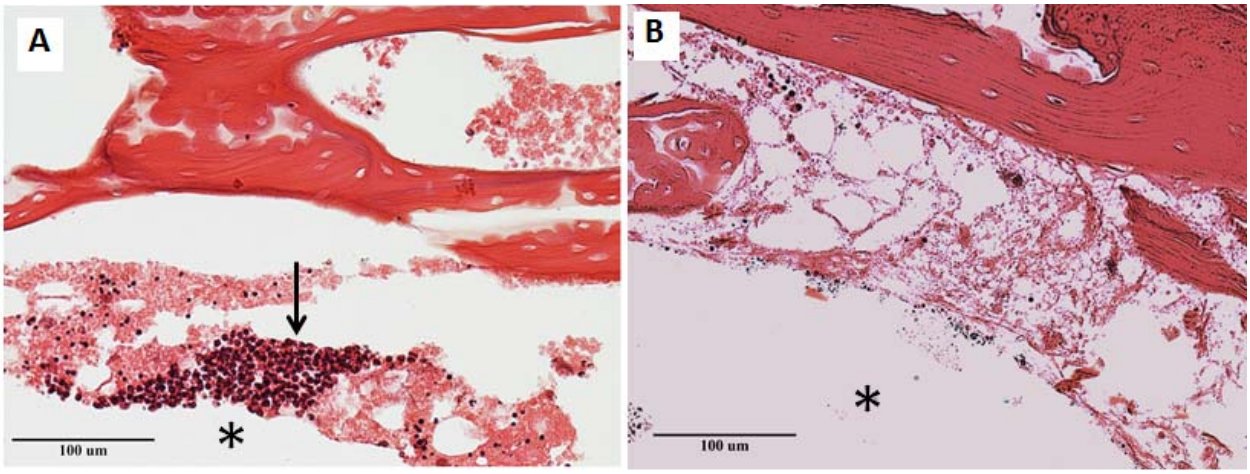
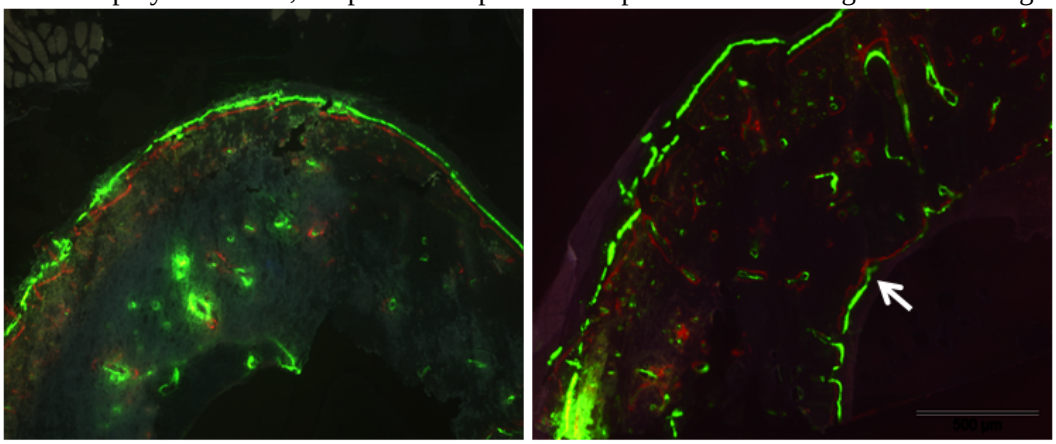


Figure 5. Histological microphotographs of femora of rats filled with Simplex P (A) or DY5-1TOSU cement (B) at week one PO. *=cement area, arrow points to inflammatory cells.

Endosteal fluoresence double-labeling was observed in DY5-1TOSU group, in contrast to no endosteal fluorescent double-labeling in simplex P group (Figure 6). We are increasing the sample size to determine statistical significance. We have added six Simplex P samples and eight DY5-1TOSU samples harvested at 8 weeks PO. The femurs were longitudinally split and dehydrated in serial ethanol solution. The bone cements in the femur were removed with methyl ethyl ketone. The methyl ethyl ketone was washed off in serial ethanol solution. The samples were dehydrated in serial ethanol solution and infiltrated with acetone and infiltration solution for 5 days. The samples are in the embedding solution in -20 ^{o}C freezer. After polymerization, the plastic samples will be processed-trimming and sectioning.



Simplex P **DY5-1TOSU**

Figure 6. Fluorochrome labeling of cortical bone of rat femur filled with Simplex P or DY5-1TOSU silorane cement. The periosteal and endosteal double labeling were observed in DY5-1TOSU group. The arrow points to endosteal fluorescence double labeling. The red line: alizarin, the green line: calcein.

Biomechanical testing: The rats were sacrificed 8 weeks PO and the femora of rats were harvested. The pull-out test was performed. The pull-out strength of the femora filled with Simplex P was 2.79 MPa, 0.25 for M12-ECHE, 0.29 for DY5-ECHE and 0.62 for DY5-1TOSU (Figure 7). The values of pull-out strength of silorane-based cements are much lower than that of Simplex P. Therefore a series of studies were initiated to improve pull-out strength *in vivo* including conversion to a putty, an increase in filler, coating of titanium rods, and dessication of the resin and monomer before use.

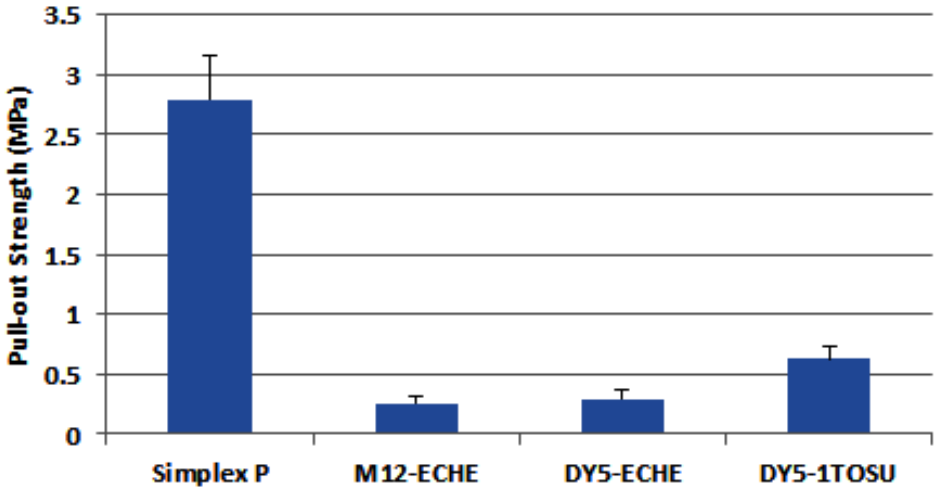


Figure 7. Pull-out strength of femora of rats filled with different bone cements at 8 weeks PO. *This was not as expected.* These results suggested that fluids in the *in vivo* environment were most likely influencing polymerization of the silorane bone cement around the titanium rods.

2). Rat in vivo study to determine if converting the DY5-1TOSU to a putty will improve pull-out strength.

Two 8-month-old rats were used. The rats were anesthetized and operated on under aseptic conditions. Briefly, the left knee was exposed and the bone marrow was disrupted. The marrow cavity was irrigated and filled with Simplex P, putty DY5-1TOSU and DY5-1TOSU, respectively. Then a titanium rod without saline-wash was inserted into cement. The capsule and skin were sutured. The animals were sacrificed at 24 hrs PO. The femurs were harvested and immediately tested biomechanically. In the DY5-1TOSU groups, the rods were pulled out of DY5-1TOSU cement. The pull-out strength of putty DY5-1TOSU is 1.3 MPa. The pull-out strength of the original DY5-1TOSU is 0.5 MPa. Therefore, the pull-out strength of the DY5-1TOSU was increased over 100% by changing the consistency to a putty. In the Simplex P group, when the pull-out strength reached 5.7 MPa, The bone was broken and the rod with cement came out of bone. Then the implant was re-anchored and continually pulled out until the rod separated from the cement. The eventual pull-out strength reached 14.9 MPa. The graph is as follows:

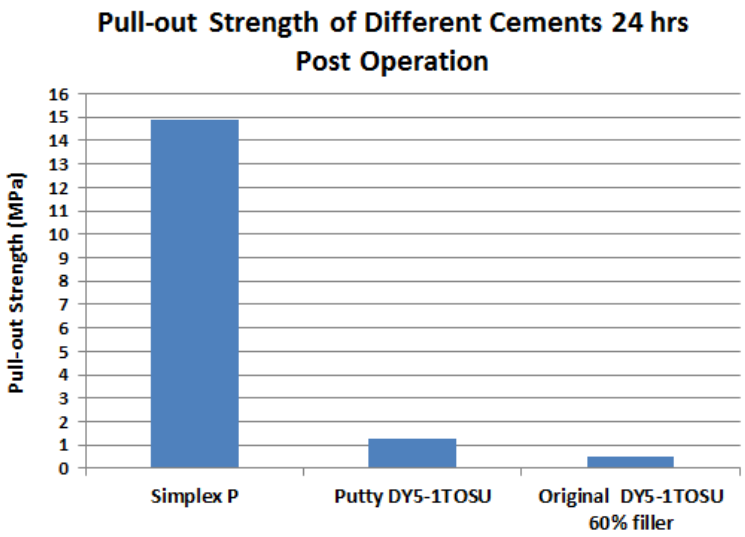


Figure 8. Pull-out strength of original and putty DY5-1TOSU bone cements 24 hrs PO.

3). In vivo determination of pull-out strength of rods with and without phosphonate ester coating. The animals were sacrificed 2 weeks PO.

In order to improve the pull-out strength, the titanium rod was coated with phosphonate ester. In this group study, two 8-month-old rats were used. The surgical procedures were same as above. The femur of rat was filled with DY5-1TOSU cement and a rod coated with phosphonate ester was inserted. The rats were sacrificed two weeks PO. The biomechanical test was performed. The pull-out strength was 0.62 MPa. There was no difference between the coated rod and uncoated rod (figure 9).

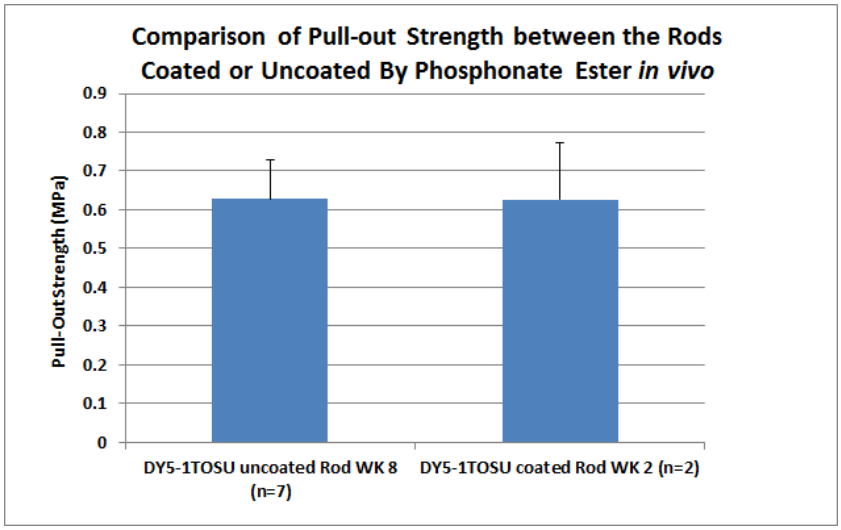


Figure 9. Pull-out Strength of original DY5-1TOSU cement with rods coated or uncoated with phosphonate ester.

4). Rat in vivo study to determine if percent filler will improve pull-out strength.

Six 8-month-old rats were used. Both legs were shaved and disinfected with betadine. The skin was incised. The both femurs were operated on under aseptic condition (n=3/formulation). The knee joint was

exposed and 2.2 mm of hole was created between the femoral condyles. The bone marrow was disrupted and filled with Simplex P, putty DY5-1TOSU 74% filler, putty DY5-1TOSU 65% filler and original DY5-1TOSU 60% filler, respectively. Then a titanium rod was inserted. The animals were sacrificed at one week PO. The femurs were harvested and immediately tested biomechanically. The pull-out strength for Simplex P was 6.75 MPa, 1.92 MPa for Putty DY5-1TOSU 74% filler, 3.75 MPa for Putty DY5-1TOSU 65% filler, and 2.59 MPa for original DY5-1TOSU 60% filler. Therefore, 65% filler improved pull out strength.

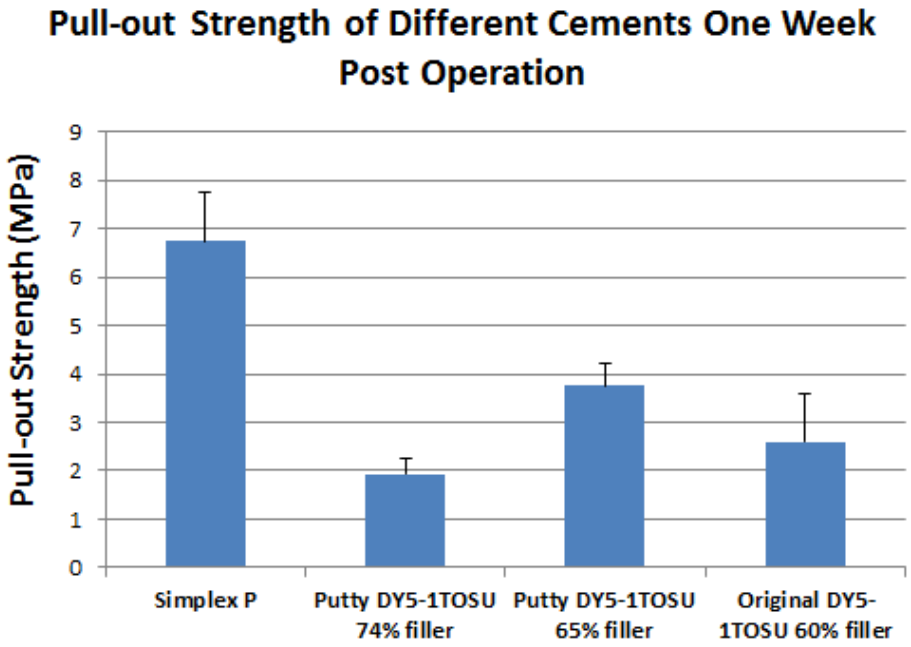


Figure 10. Pull-out strength of different bone cements one week PO.

5). Rat in vivo study to determine if preparation of highly dessicated silorane and filler will improve pull-out strength.

Fifteen one-year-old rats were used. The right leg was shaved and disinfected with betadine. The skin of the knee joint was incised. The right femur was operated on under aseptic condition. The knee joint was exposed and 2.2 mm of hole was created between the femoral condyles. The bone marrow was disrupted and reamed, irrigated with phosphate buffered saline, and filled with Simplex P (n=3), original DY5-1TOSU 60% filler (n=3), dry original DY5-1TOSU 60% filler (n=3), dry putty DY5-1TOSU 65% filler (n=6), respectively. Then a dried titanium rod was inserted into the cement-filled femur (n=3/formalation) in first four groups, and in fifth group, a dried titanium rod pre-dipped with dry putty DY5-1TOSU 65% filler was inserted into dry putty DY5-1TOSU 65% filler cement-filled femur (n=3). The animals were sacrificed at one week PO. The femurs were harvested and immediately tested biomechanically. The pull-out strength for Simplex P was 4.08 MPa, 1.68 MPa for original DY5-1TOSU 60% filler, 2.58 MPa for dry original DY5-1TOSU 60% filler, and 4.44 MPa for dry Putty DY5-1TOSU 65% filler and 4.75 MPa for dry Putty DY5-1TOSU 65% filler with pre-dipped rod. Therefore dessicating the resin and monomer before use improved pull-out strength to the same level as the Simplex P control. No differences were observed between pre-coating or non coated titanium rods.

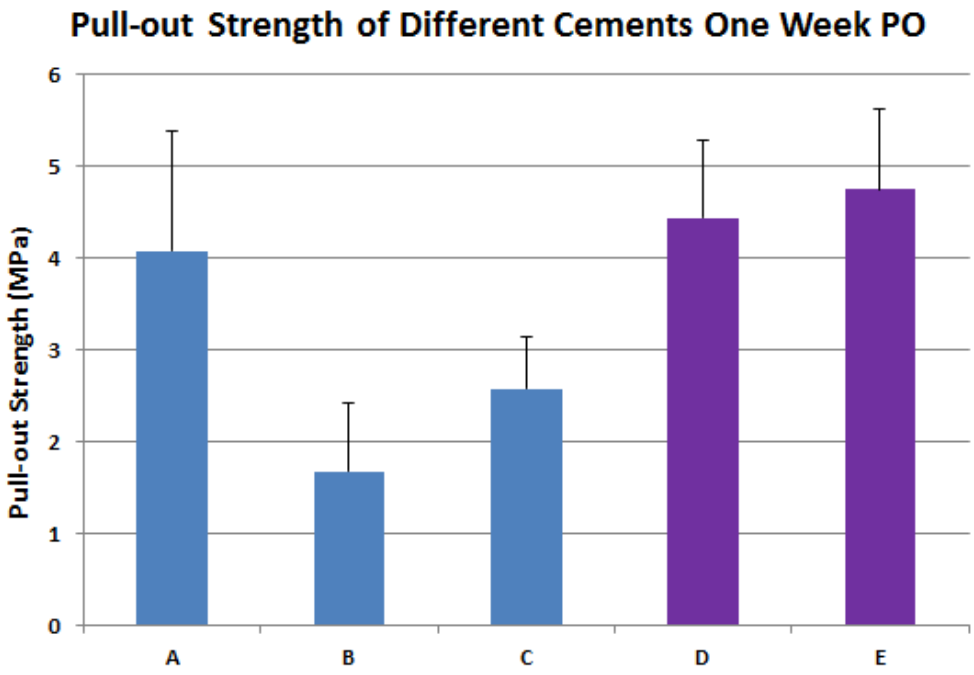


Figure 11. Pull-out strength of different bone cements one week PO. A: Simplex P, B: original DY5-1TOSU with 60% glass filler, C: dry original DY5-1TOSU with 60% glass filler, D: dry putty DY5-1TOSU with 65% glass filler, E: dry dipped putty DY5-1TOSU with 65% glass filler.

In summary, *in vivo*, the silorane bone cements are non-toxic, non-inflammatory, and do not inhibit bone formation in contrast to commercially available bone cement which is toxic. However, these silorane bone cements must remain dessicated before use to insure ideal pull out strength.

FY10 Task 3. Determine the biological response to silorane bone cement in animal models, Subtask 3b. Large Animal (Swine) Model. Months 24-30.

This task is starting this month. Scale up of DY5-1TOSU is underway. The silorane bone cement will be tested *ex vivo* in swine femori before proceeding into the live animals.

Comments on administrative and logistical matters.

We were very surprised to observe poor pull-out strengths for the silorane in the first *in vivo* rat study (Figure 7). The mimic pull out tests showed equivalent pull-out strength between simplex P and the silorane bone cements and whereas the pullout strengths for the siloranes was slightly lower that simplex P in the *ex vivo* rat femoral model, (See year one report), we still did not anticipate the *in vivo* results. Since then we have determined that water interferes with the bonding of the silorane bone cement to the titanium rod.

We have identified dessicated silorane material and dessicated 65% filler to be the optimal silorane bone cement which will be used for the large animal experiments (Figure 11).

KEY RESEARCH ACCOMPLISHMENTS:

- Discovered that water interferes with the appropriate polymerization and bonding of the silorane bone cements to titanium.

- Developed a silorane bone cement that has equivalent pull-out strength to commercially available bone cement, but is non-toxic, non-inflammatory, non-exothermic, has low shrinkage, and is potentially osteogenic.

CONCLUSIONS*:*

We have developed a novel silorane bone cement with excellent properties that is ready for in vivo large animal testing. While conducting the animal studies it will be determined if wear debris from this cement will have any inflammatory or osteoclast activation/resorption properties. We are hopeful that this technology will soon be licensed. We also plan a resubmission of the SBIR for the commercialization of the silorane bone cement. In contrast to commercially available bone cement which is toxic, the silorane bone cement does not cause any weight loss, bone loss, or inflammation in vivo. With the improved biocompatibility, reduced exothermicity, good handling properties, incorporation of antibiotics/growth factors, and potential for osseointegration/osseoinduction, this material has potential to be used for screw augmentation, total hip/knee joint replacement, and other orthopedic and dental applications. The reduced curing temperature of approximately 26° C of the dual initiated silorane composite makes it possible to carry and deliver a wide range of antibiotics and potentially growth factors, which previously could not be used in PMMA bone cements. We have overcome our previous issues with strength to produce a material that is on par with commercial bone cement. The development of the silorane bone cement is very promising for application for human use.

PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS:

Dual-initiated Silorane Formulations for Use as a Bone Cement Alternative, Kilway, K. V.*; Eick, J. D.; Bi, L.; Weiler, R. A.; Miller, B. D.; Bunnell, T. J.; Melander J. R.; Schuman, T. P.; Bonewald, L. F., Poster # 1232, Orthopaedic Research Society 2013 Annual Meeting, San Antonio, TX, January 26-29, 2013.

Novel Silorane Bone Cements Exhibit Similar Mechanical Properties but None of the in vivo Inflammatory Effects of Commercial Bone Cement. Lianxiang Bi*1, David Eick1, Kathleen Kilway1, Rachel Weiler1, Bradley Miller1, Thomas Schuman2, Lynda Bonewald1. 1University of Missouri Kansas City, USA, 2Missouri University of Science & Technology, USA SU0065 ASBMR, Baltimore, MD, October 4-7, 2013.

The Optimization and Effect of a Platinum Catalyst on the Mechanical and Handling Properties of Novel Silorane Bone Cements while maintaining Osteogenic Capacity. Kathleen Kilway*1, Rachel Weiler1, Lianxiang Bi1, J. David Eick1, Bradley Miller1, Thomas Schuman2, Lynda Bonewald1. 1University of Missouri – Kansas City, USA, 2Missouri University of Science & Technology, USA MO0054, ASBMR, Baltimore, MD, October 4-7, 2013.

Bunnell,T.J.; Bi,L.; Bonewald,L., "Evaluation of Different Silorane-Based New Bone Cements," Abstract #846, International Association for Dental Research/American Association for Dental Research, 91st General Session, Seattle, WA, March 20-23, 2013.

INVENTIONS, PATENTS AND LICENSES: A patent cooperative treaty (PCT) has been published for the innovative chemical initiator systems by UMKC and Nanova will have an exclusive license (still under negotiation).

REPORTABLE OUTCOMES: We have developed a silorane bone cement that has equivalent pull-out strength to commercially available bone cement, but is non-toxic, non-inflammatory, non-exothermic, low shrinkage, and potentially osteogenic that will hopefully be commercialized.

OTHER ACHIEVEMENTS:

Degrees obtained that are supported by this award:
Daniel Rodman – undergraduate researcher, BA in Chemistry graduated in July 2012, (still worked for us through October 2012) now employed by SpecChem

Katelyn Kephart - undergraduate researcher, BA in Chemistry graduated May 2013, employed by Cerner

Khristle Tolbert - undergraduate researcher, BS in Chemistry graduated May 2013

James Cash - undergraduate researcher, BA in Chemistry, graduated July 2012 (still worked for us through December 2012) now attending chiropractic school at Logan College of Chiropractic University Programs in St. Louis, MO

Leila Suleiman - undergraduate researcher (from June 2012 – present), BS in Chemistry, will be graduating December 2013

Employment received based on experience/training supported by this award.

Bradley Miller – IPhD student (coordinating unit Chemistry with Pharmaceutical Sciences and Oral Biology as co-disciplines- to defend either this semester or next semester), visiting lecturer at William Jewell, Liberty, MO, August 1, 2013 – July 30, 2014

REFERENCES: none

APPENDICES: none